Dissertation on

STUDY OF THE EFFECT OF GRID LASER PHOTOCOAGULATION ON CONTRAST SENSITIVITY IN PATIENTS WITH DIABETIC MACULAR ODEMA

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CERTIFICATE

This is to certify that this dissertation entitled **"STUDY OF THE EFFECT OF GRID LASER PHOTOCOAGULATION ON CONTRAST SENSITIVITY IN DIABETIC MACULAR ODEMA "** is a bonafide record of the research work done by **Dr. RAMYA.M.,** post graduate in Regional Institute of Ophthalmology Government Ophthalmic Hospital, Madras Medical College and Research Institute, ,Chennai-03, in partial fulfillment of the regulations laid down by The Tamil Nadu Dr.M.G.R. Medical University for the award of M.S. Ophthalmology Branch III, under my guidance and supervision during the academic years 2009-2012.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"STUDY OF THE EFFECT OF GRID LASER PHOTOCOAGULATION ON CONTRAST SENSITIVITY IN DIABETIC MACULAR ODEMA "** is a bonafide and genuine research work carried out by me under the guidance of our Prof Dr Sulaiman and Prof Dr Revathy.

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Place : Signature

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CONTENTS

PART - I

LIST OF ABBREVIATIONS

NPDR	-	Non proliferative diabetic retinopathy
CSME	-	Clinically significant macular edema
CME	-	Cystoid macular edema
DME	-	Diabetic Macular edema
OCT	-	Optical coherence tomography
FFA	-	Fundus fluorescin angiography
IVTA	-	Intra vitreal triamcinolone
VEGF	-	Vascular endothelial growth factor
ILM	-	Internal Limiting Membrane
IRMA	-	Intra retinal microvascular anomaly

INTRODUCTION

Contrast sensitivity is an important aspect of visual function and is even more important for ordinary daily tasks than visual acuity.

Contrast sensitivity function may be deteriorated to a significant level in diabetic retinopathy, especially in diabetic macular edema. Diabetic macular edema is a microvascular complication of diabetes mellitus defined as retinal thickening resulting from the accumulation of fluid in the retina. When it is associated with hard exudates, both retinal damage and permanent visual loss will occur.

Diabetic macular Odema is one of the major causes for moderate vision loss in diabetic patients. Laser photocoagulation is the treatment modality for DME either focal or grid laser is done which reduces the odema thus improving the vision and contrast sensitivity. The objective of this study was to determine the impact of macular laser photocoagulation as the standard treatment of clinically significant macular edema on contrast sensitivity.

ANATOMY OF THE MACULA

Macula is the optical, functional and organic focal point of the eye. It is the precise visual functions of acuity, form sense, colour differentiation and stereopsis.

According to Wolff, the macula is an oval zone of yellow coloration within the central retina approximately 5mm in diameter. The yellow colour of the macula is probably due to the presence of carotenoid pigment xanthophll in the ganglion cells and bipolar cells in this area.

The side walls of the macula is the clivus which slopes gently towards the fovea centralis. Fovea is the center of the area centralis and is located 4mm temporal to the center of the optic disc and 0.8mm below the horizontal meridian. Its thickness is 0.25mm, diameter is 1.85mm and it corresponds to 5 degrees of visual field. Foveola is at the center of the fovea where the retinal layers are thinner. It is of thickness, 0.35mm diameter and it corresponds to 1 degrees of visual field. It is the area of highest visual acuity because of the sole presence of cone receptors and its avascularity. It appears deeper red than the adjacent retina because of the rich choroidal circulation and abundant choriocapillaris.

HISTOPATHOLOGY

The retina as such has 10 layers which are as follows

1. Retinal pigment epithelium
2. Photoreceptors layer of rods and cones
3. External limiting membrane
4. Outer nuclear layer
5. Outer plexiform layer
6. Inner nuclear layer
7. Inner plexiform layer
8. Ganglion cell layer
9. Nerve fibre layer
10. Internal limting membrane

At the fovea the only layers present are the

1. Retinal pigment epithelium
2. Photoreceptors layer only cones
3. External limiting membrane
4. Outer nuclear layer
5. Henles layer
6. Internal limiting membrane

Thus the fovea has no inner nuclear layer, inner plexiform layer, or no ganglion cell layer and practically no nerve fibre layer.

At the macula ganglion cells are much more than elsewhere in the retina, being arranged in several layers.

Outer plexiform layer is made up of arborisation of axons of rods and cones with bipolar cell dendrites, it also includes muller's fibres and horizontal cell processes. This layer has reticular structure but as the macula is approached it takes a fibrous structure called 'henle's fibre layer'. The fibres run at first vertically then obliquely near the macula and finally parallel to the surface. This layer is thickest at the macula but almost absent at the fovea. There is also progressive disappearance of the rods[1] The RPE and choriocapillaries are thicker than at the macula. This is important since the macula has no retinal blood vessels. At the fovea the layers of the retina are spread aside so that light may fall directly on the cones.

Each cone is connected to only one ganglion cell (in other area each ganglion cell connects upto 100 rods). At the center of the fovea cone cells are located in a 50u diameter area and are separated from each other by relatively wide spaces of watery cytoplasm belonging to muller's fibres. The thinness of the basal lamina and the watery cytoplasm allow the light to pass through.[2]

Anatomical peculiarities of macula causing an exaggerated response to pathological process

Peculiar susceptibility of the macula to a number of pathological process both local and generalized is called' exaggerated response' of the macula.[3] The causes for this are listed below-

1. Vascular supply:

The arcade arrangement of the capillaries which arise as terminal parts of an end artery system, together with the central avascular zone make fovea a water shed. Local impairment of metabolism, whether from disturbances in perfusion and accumulation of metabolites or from the effects of capillary damage, lead to extracellular fluid accumulation at a quicker rate than what can be absorbed.

2. Tissue architecture

The processes of muller's cells run horizontally in the Outer plexiform layer, hence retina loses its compact nature and this laxity enables large quantities of extracellular fluid or exudates to be accommodated in the macular region leading to characteristic cystoids macular odema.

3. Cellular constituents

The ganglion cells have high metabolic rate and their dysfunction due to any cause leads to rapid accumulation of tissue metabolites. Most of them have vasodilator effect and this along with underlying hypoxia can lead to CME.

4. Internal limiting membrane

The vitreous is an excellent diffusing medium and the ILM provides little additional interference to the progress of toxic substances arising from the iris, peripheral choroid and parsplana. These substances may traverse the vitreous and because of the thinness and adherence of the ILM in the foveal region, may preferentially disturb the function of the cells which are highly concentrated around foveal rim, and also affect the macular permeability

5. Choroid and RPE

The macular choroid and the RPE are also the preferential sites for degenerative changes which may be hereditary, toxic or atherosclerotic. There is a predisposition for choroidal vascular diseases with decompensation and hemorrhage in the central area which is

thought to be because RPE in the fovea is very active metabolically hyperactivity along with the special haemodynamic effects of the narrow choroidal capillaries may lead to increased susceptibility.

PATHOGENESIS OF DIABETIC MACULAR ODEMA (DME)

Diabetic macular odema(DME)

It is the most common cause of moderate visual impairment in patients with NPDR. It occurs as a result of the blood retinal barrier which leads to accumulation of fluid within the intraretinal layers of the macula . Its incidence increases with the type of diabetes(more common in type 2) duration of DM, age of onset, uncontrolled DM, associated risk factors like hypertension, hyperlipidemia, anaemia, nephropathy.

Epidemiology of DME

Macular odema increases 3% in mild NPDR, 38% in severe NPDR and 71% in PDR.

1. Blood retinal barrier:(BRB)

The common pathway that results in DME is disruption of BRB. It compartmentalizes the the neurosensory retina from the vascular component of the eye. It consists of two major components: the outer barrier and inner barrier. The inner barrier is biological unit formed by tight junctional complexes between retinal vascular endothelium and

glial cells and the outer BRB is formed by tight junctions between the retinal pigment epithelial cells. The permeability of both components of BRB may be increased in diabetic patients.

The mechanism of the BRB breakdown is multifactorial. It is secondary to changes in the tight junctions, pericyte losss, endothelial loss, retinal vascular endothelium and RPE cells, activation of AGE receptor, down regulation of glial cell derived neurotrophic factor, retinal vessel dilation and vitreoretinal traction

2. Vaso active factors:

Sustained hyperglycemia affects several vasoactive factors eg; VEGF, protein kinase C, heparin, angiotensin II, PEDF, metalloproteinases and biochemical pathways in diabetes, which may influence the development of structural and functional changes in diabetic retinopathy. Hypoxia and hyperglycemia upregulate VEGF production in diabetic retinopathy which in turn increases vasopermeability by activating PKC, hyperglycemia increase PKC and angiotensin II both of which cause vasoconstriction and worsening of hypoxia by their effect on endothelins.

3. Vitreoretinal interface:

DME may be exacerbated due to persistent vitreomacular traction by residual cortical vitreous on the macula after PVD. Thickened and taut posterior hyaloid that may or may not be adherent to ILM, macular traction due to tractional proliferative membranes or loculation of cytokines in the pre macular vitreous pocket lead to DME

Clinical features

Diabetic macular odema has following features

1. Thickening of macula
2. Blurring of underlying choroidal vascular pattern
3. Loss of foveolar light reflex if foveola is involved
4. Cystoids spaces
5. Lipid exudation from leaking microaneurysms forming circinate retinopathy

DIAGNOSIS OF DME

This is best detected by slit lamp biomicroscopy with + 90 D, 78D ,or macular contact lens. Fundus fluorescein angiography is standard method used to evaluate patients with DME that is sensitive for qualitative detection of fluid leakage. OCT aids in quantification of retinal thickening and for classification.

OCT has its role in diagnosis and quantification of retinal thickening, macular volume, retinal morphology and vitreoretinal relationship in DME. It is also important in defining the indication of surgery, determining the prognosis and quantifying the response to therapy.The main pathology in DME is accumulation of fluid intraretinally. This is seen as reduced backscattering seen most commonly in the Outer retinal layers.[3]

Clinically significant macular odema(CSME)

Thickening of the retina< 500 microns from the center of the macula. Hard exudates with thickening of the adjacent retina located 500 microns from the center of the macula. A zone of retinal thickening, 1 disc area or larger in size located 1 disc diameter from the center of the macula

CLINICALLY SIGNIFICANT MACULAR ODEMA(CSME)

Fig.1 mild NPDR

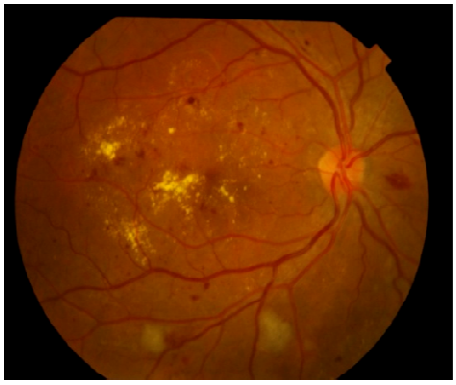


Fig.2 moderate NPDR

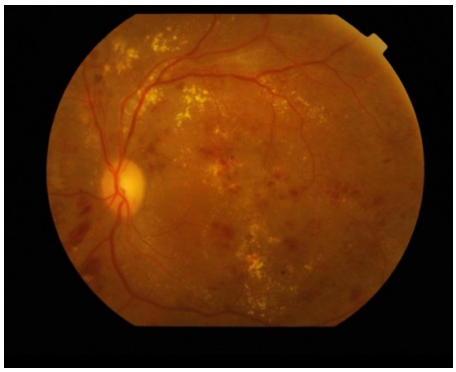


Fig.3 severe NPDR

Fig.4 Hard exudates on the fovea

FFA CLASSIFICATION

1. Focal maculopathy:

Areas of focal leakage from microaneuyrsms and dilated capillary segments. These focal areas of thickening are delinated from adjacent healthy retina by complete or partial ring of hard exudates. Focal odema show leakage in the late phase

2. Diffuse maculopathy

Areas of leakage from IRMA, retinal capillary bed Breakdown of blood retinal barrier with from microaneurysm and dilated capillary bed throughout posterior retina causes diffuse odema. It differs from focal odema by:

1. Diffuse odema usually not associated with hard exudates.
2. Even when odema resolves spontaneously it does not leave hard exudates
3. Cystoids spaces develop more commonly in DME. It is visible clinically, but seen better in late phase of FFA and OCT as hyperreflective septa
4. Mostly bilaterally symmetrical

5. May disappear spontaneously at the same time in both eyes even without laser only to reappear spontaneously.

6. Systemic factors associated with exacerbation is hypertension, hyperlipidemia, anemia

3. Ischemia maculopathy

Ischemia type of lesion has the following

- Enlargement of FAZ

- irregularities of FAZ

- capillary budding FAZ

- widening of intercapillary space and capillary drop out in the perifoveal area.

4.**Mixed maculopathy-** It is a combination of focal maculopathy

and diffuse maculopathy.

FFA CLASSIFICATION

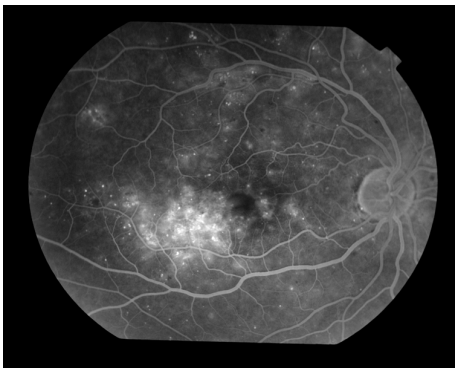


Fig 5 focal maculopathy

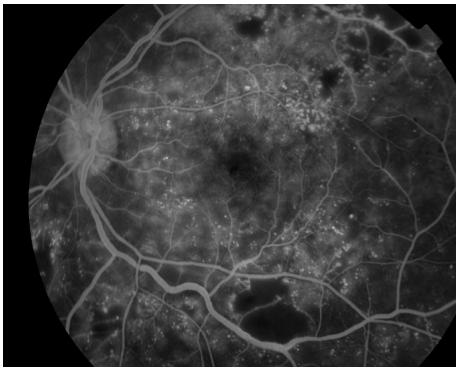


Fig -6 Diffuse maculopathy

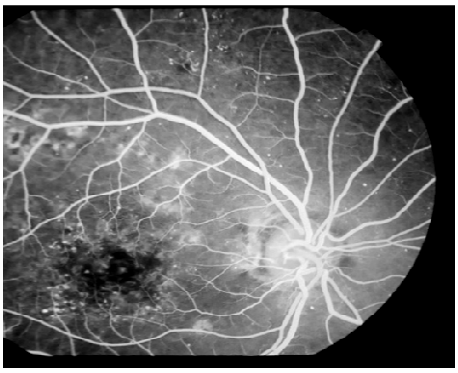


Fig 7 Ischemic maculopathy

OCT CLASSIFICATION

1. **Spongy odema:** It is the most common presentation, Cross sectional scans show swelling of the retina giving spongy appearance with increased retinal thickness. Back scattering seen from intra retinal fluid accumulation. It is confined mostly in outer retinal layers while internal layers maintain their normal reflectivity.[5]
2. **Cystoid odema:**It is the second most common which shows Intra retinal cystoids spaces. Involves variable depth of retina has intervening septa in between. Progresses gradually to involve the whole of the retinal thickness.
3. **Serous detachment-** It is seen as a hyporeflective area between nerosensory retina and RPE.
4. **Taut posterior hyaloid membrane:** Taut thickened shiny glistening hyper reflective membrane with striations on retina over the posterior pole with attachment to the disc and top of the elevated macular surface. Retinal thickness is greatly increased with intra retinal hypo reflective cyst like cavities. May also present as macular odema with foveal detachment
5. **Vitreomacular traction-** it is seen as a hyporeflective membrane extending from the vitreous to the macula.It causes detachment of fovea. Its an indication for pars plana vitrectomy. Laser will worsen macular odema.[5]

Treatment of DME

Laser therapy has been part part of treatment since mid 1980's. The goal of macular laser photocoagulation is to limit vascular leakage through focal laser burns of leaking microaneuyrsm or grid laser burns in areas of diffuse break down of the blood retinal barrier.

Frequency doubled Nd :Yag laser (532nm) is laser choice in the management of DME. The laser is to photocoagulate leaking microaneuyrsm 500u away from the centre of macula Grid laser done for patients with diffuse macular odema using double frequency Nd yag laser 532 nm. Contact lens used Goldman 3 mirror lens or Mainster high magnification or standard.[5]

- Duration- 100- 200ms
- Spot size- 50 – 100 microns
- Intensity-mild to moderate
- 1 burn width apart, 500u from centre of macula and 500u from temporal margin of disc.

CONTRAST SENSITIVITY

Contrast is the ability to perceive slight changes in luminance between regions that are not separated by definite borders. Loss of Contrast sensitivity is more important and disturbing for the patient than is the loss of visual acuity.[6]

Contrast sensitivity determines how well a person sees faces in a crowd, read a newspaper or drives an automobile at night. These are questions pertaining to person's quality of life and quality of vision. To obtain answers to these questions we need to assess the person's functional vision. The conventional measurement of visual function like snellen's acuity, colour vision and visual fields do not provide us with a complete picture of patient's quality of vision. Snellen's acuity is measure of resolution, the smallest size black on white letters a person can read. But objects in the real world come with a wide a range of contrast.[6]

Types of Contrast sensitivity

1. **Spatial Contrast sensitivity :** It refers to detection of striped patterns at various levels of contrast and spatial frequencies. Patient is presented with sine wave gratings of parallel light and dark bands(arden gratings) and is asked to tell the minimum contrast at which the bars can be seen at each frequency.[7]

2. **Temporal Contrast sensitivity:** Here the contrast sensitivity function is generated for time related (temporal) processing in the visual system by presenting a uniform target field modulated sinusoidal in time rather than as a function of spatial position. [7]

Measuring contrast sensitivity

There are three variables in the measuring contrast Sensitivity

The average amount of light reflected depend on:

1. Illumination of paper and darkness of ink
2. Degree of blackness in relation to the white background i.e contrast
3. The distance between the grating periods or cycles per degree of visual angle

Arden gratings

The Arden plates introduced formally in 1978 consisted of booklet of seven plates with sine wave gratings ranging from 0.4 to 0.6 cpd at a distance of 57cms. Sine wave gratings, which are alternating dark and light bands are used to assess the function of contrast sensitivity. It was gold standard target for evaluating contrast sensitivity because they test individual visual channels in the most sensitive. Due to the high false positive rates associated with set up newer modalities were divised. [8]

The Cambridge low contrast grating:

It is simple and rapid test for contrast sensitivity. It is a set of ten plates containing gratings in a spiral bound booklet. To perform the test booklet is hung on a wall at distance of 6m. The pages are presented in pairs one above the other. One page in each pair contains gratings and the other is blank. The subject is simply required to choose which page, top or bottom contains gratings. The pages are shown in order of descending contrast and are stopped when the first error is made.[9]

Vis Tech chart

The first grating chart that could be mounted on wall is Vis Tech chart. This consists of six rows of sine wave grating patches tilted in different orientations used at distance of 3m from the subject. In this test contrast is assessed at several spatial frequencies and subject has to identify the orientation of the grating i.e whether vertical or 15 degree clockwise and anti clockwise. The CSV-100(vector vision) is another grating based chart. It has an retro-illumination system.[9]

Contrast Sensitivity Chart

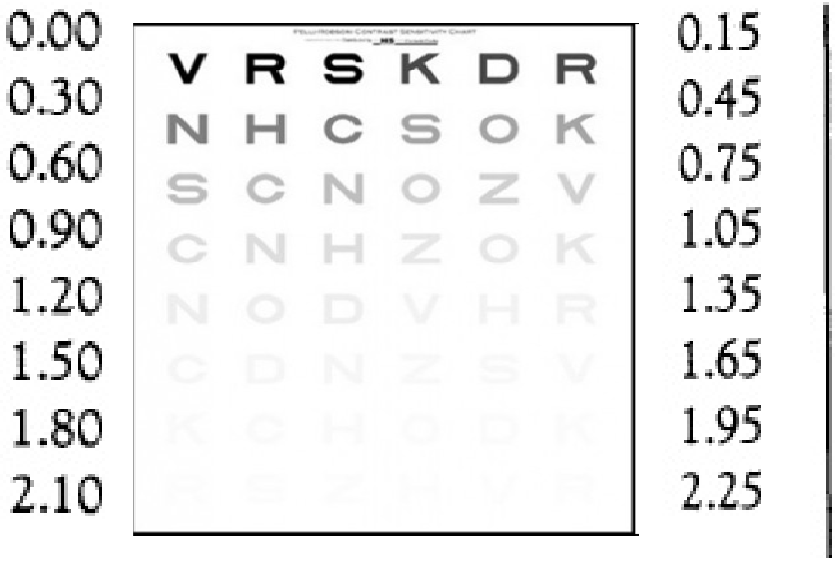


Fig 8 showing Pelli Robson chart

Visual acuity Chart

Fig 9 showing ETDRS chart

The Pelli - Robson Contrast Sensitivity Charts

It consists of 8 rows of six letters of constant size arranged in 16 groups of three. This chart consists of letter which subtend angle of 3 degree at a distance of 1m. All the letters are of same size but decreasing in contrast every group of 3. Contrast of the test letters decreases from near 100% at the top to less than 1%. When contrast is 0%, there is no edge between the two adjacent areas—that is, no pattern is physically present. For any value greater than 0%, an edge exists though it may or may not be visible, depending on the image-processing capabilities of the detector.[6] At the bottom of the chart in 0.15-log unit sensitivity steps for each triplet of letters. The log contrast sensitivity varies from 0.00 to 2.25.[7]

The chart was used at 1 m at a mean luminance of 85 cd/m2 (i.e.illumination of approx 280 lux).The dimension is 97 x 82 cm[8].While recording subject sits directly in front of chart at distance of 1m with best correction. The subject is made to name or outline each letter on the chart starting from the upper left corner and reading horizontally across the line each eye tested separately. Subject is made to guess even when he or she believes that the letters are invisible. The test is concluded when the subject guesses two of the three letters of the triplet

incorrectly. The subject's sensitivity is indicated by the finest triplet for which two of the three letters are named correctly.[8]

The chart is good test–retest reliability, availability of published normative data have led to its frequent choice for epidemiologic studies. Contrast is expressed as a percentage, from 0% to 100%.

ETDRS CHART

ETDRS acuity testing has become the standard for testing visual acuity, replacing the Snellen. ETDRS stands for Early Treatment Diabetic Retinopathy Study. The ETDRS acuity test was developed to aid in evaluating the changes in vision following panretinal photocoagulation in patients with diabetic retinopathy The ETDRS test is designed to eliminate inaccuracies in the Snellen acuity tests.[10]

Fallacies in Snellen chart

- Snellen acuity test has a variable size and number of letters per row.
- Poor vision lines have 1 or 2 letters, good vision lines have 8 letters Therefore, if the results of a study showed that the patients "gained three letters of acuity," the results could indicate the gain of a full acuity line.
- The individual lines on the Snellen acuity test are not equally spaced. For example, the change from the 20/25 line to the 20/20 line is a 20% change, while the change from the 20/30 line to the 20/25 line is a 16% change. Crowding phenomenon- when letters are spaced too closely there is an effect from adjacent contours that reduces the visual acuity

- Letters are not always of same legibility, few letters are easier to read (C,D,E,O,G) than (A,J,L)
- Lack of standardised progression between lines missing of 1 letter on good acuity lines has less effect than missing 1 letter in poor vision lines.[11]

ETDRS Design

The ETDRS test incorporates specific design criteria to make it more accurate than the Snellen acuity tests. These include:

- Same number of letters per row (five letters per row) 14 rows total of 70 letters.
- There is consistent spacing between the letters and rows proportional to the size of the letter
- Equal spacing of the rows on a log scale (the rows are separated by 0.1 log unit). Spacing between letters is equal to the width of letter.
- Equal spacing of the letters on a log scale. Spacing between row equal to the height of next row letter.

- Equal lo interval (ratio of 1.26X) in the progression of letter size between lines. The letters double in size in every third line.[11]

ETDRS Standardization

Using the best correction in a trial frame, ETDRS chart was placed 4 meters from the patient in a back-illuminated stand. The ETDRS chart was printed with high-contrast lettering on a translucent white polystyrene panel lit from behind and displayed in a standard light box. The light box was illuminated by two fluorescent lamps with a reusable fenestrated sleeve (diffuser) that produced a chart luminance, measured by a digital light meter of 168 cd/m2, which is in compliance with recommendations of the ETDRS protocol (80 to 320 cd/m2).

Scoring the ETDRS Chart

ETDRS Scoring Method 1:

The patient starts are the top of the chart and begins to read down the chart. The patient reads down the chart until he or she reaches a row where a minimum of three letters on a line cannot be read. The patient is scored by how many letters could be correctly identified. If a patient could not read the largest letters at 4 meters, then the chart was moved 50% closer to the patient (4 meters to 2 meters, or 2 meters to 1

meter).ETDRS Score is a letter score is calculated based on the number of letters that can be correctly identified from specified distances. Higher letter scores correspond to better visual acuity. Lower letter scores mean poorer visual acuity.[12]

ETDRS Letter Score*	**Snellen Visual Acuity Equivalent**
25	6/95
30	6/76
35	6/60
40	6/48
45	6/38
50	6/30
55	6/24
60	6/19
65	6/15
70	6/12
75	6/10
80	6/8
85	6/6

*** ETDRS** Score = number of letters read plus 30

ETDRS Scoring Method 2:

The ETDRS charts were originally used in ETDRS studies where patients had relatively poor vision. For these patients, a second scoring method is used. The patient starts on the last row where he or she can read all of the letters, and then reads down until he or she reaches a row where a minimum of three lines cannot be read. For these patients, a decimal ETDRS acuity score can be used. To calculate the decimal acuity score, follow the guidelines below. Determine the last row where the patient can correctly identify all 5 letters on that row.

Determine the log score for that row (these scores are shown in the margin of the ETDRS test, e.g. the 20/25 line has a log score of 0.1) subtract 0.02 log units for every letter that is correctly identified beyond the last row where all of the letters are correctly identified. For example, if the patient reads all of the letters correctly on the 20/30 row and then 3 letters correctly on the 20/25 row, the Log Score would be calculated as follows:

20/30 Row = 0.20 3 letters X 0.02 log/letter = - 0.06

Laser photocoagulation

During the 1940s, German ophthalmologist Meyer-Schwickerath pioneered light coagulation of the retina. The ideal wavelength is characterised by good penetration through ocular media and maximal absorption in the target tissue. Shorter wavelengths are more easily scattered, hence, red light (620 - 750 nm) has better penetration than blue light (450-495 nm). Scatter is a result of radiation absorption by tissues other than the target. The extent of laser absorption is also dependent upon the pigment composition of the target tissue. The three major ocular pigments are melanin, xanthophyll and haemoglobin. The major site of laser absorption is in the melanin containing retinal pigment epithelium (RPE) and choroid.

Xanthophyll has maximal absorption of blue light and is found predominantly in the macula. Haemoglobin has poor red light absorption but excellent blue, green and yellow light absorption. The green wavelength is superior due to minimal absorption of xanthophyll coupled with strong affinity for melanin and haemoglobin. Therefore it can be used in the macular region as well Goldmann as the periphery, and can target abnormal vessels. Yellow laser has similar to green laser, with a few advantages. This longer wavelength scatters less than green

and its absorption by haemoglobin is at least twice that of green laser, making it a more effective laser for vascular structures.Despite being considered the best wavelength to treatvascular lesions, its application has been limited by the costliness and bulkiness of krypton yellow lasers (568.2nm) Green laser is available in two systems: argon gas (514.5nm) and solid state frequency doubled Nd-YAG (532nm)and diode laser that utilise crystals and semiconductors respectively. Its beam is near infrared at 1064nm, however, frequency doubling achieved by a potassium-titanium phosphate (KTP) crystal halves the wavelength resulting in green laser. The solid-state lasers are becoming the preferred option due to their portability and ability to deliver laser in continuous and pulse mode.

Laser Wavelengths

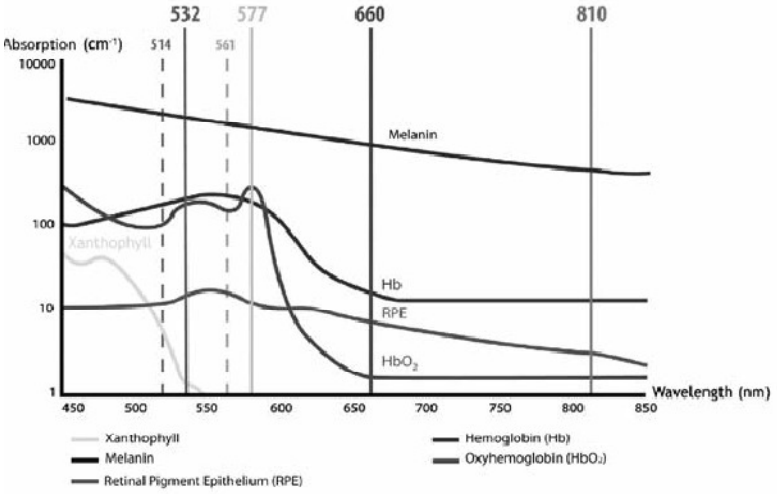


Fig 10 Graph showing absorption spectrum of various pigment in the retina

Grid laser contact lens

Fig 11 Mainster high magnification lens

Fig 12 Goldmann 3 mirror contact lens

Laser Delivery Systems

Laser photocoagulation can be applied to the retina via transpupillary laser either performed on slit lamps through specialised contact laser lenses, or with binocular indirect ophthalmoscopy through non-contact lenses.

Grid laser lenses

Contact Lens	Spot magnification	Field of view (degree)	Image
Goldmann	1.08	36	Virtual erect
Volk area centralis	0.95	82	Real inverted
Mainster high magnification	0.81	75	Real inverted
Mainster standard	1.05	90	Real inverted

Grading of laser burns

Grade 1(light)- barely visible, blanching of pigment epithelium

Grade 2(mild)-faint blanching

Grade 3(moderate)- grey, dirty white

Grade 4(severe)- dense chalky white

New and Future Innovations:

Subthreshold laser system

Retina Regeneration Therapy is currently being evaluated. It is a 532 nm laser that produces 3 nanosecond pulses. The energy level of pulses delivered are lower than those of micropulse laser with adjustable on and off times and therefore it stimulates renewal of RPE rather than destroy it. Its proposed utility is in the treatment of diabetic maculopathy. The length of these pulses needs to be shorter than the thermal relaxation time of the target tissue, that is the time required for heat to be transferred away from the irradiated tissue.

Pascal (Pattern scan laser)

Photocoagulator is a 532 nm frequency-doubled Nd:YAG solid-state laser. It is a semiautomated system that delivers laser pulses in a rapid, predetermined sequence with a variety of laser spot patterns and sizes. The main benefits are thought to be greater accuracy and faster treatment with a time reduction from 100-200 ms per burn in conventional photocoagulation compared with 10-20ms per burn with been assessed as a mode of delivering PRP and macular grid laser.

CLINICAL EVALUATION CLINICAL SIGNIFICANT MACULAR ODEMA

Visual acuity:

Loss of vision depends on the involvement of macula. It is assessed by Snellens chart, more accurate would be ETDRS chart

Colour vision:

The most common defect observed is blue yellow. The defects best detected by Fansworth munsell 100 hue test

Indirect opthalmoscope:

This technique is of special importance because it allows the examiner to integrate the view of the entire retina

Slit lamp biomicroscopy using 90 D, 78D, Goldmann 3 mirror contact lens helps to visualize stereoscopic examination of macula Threshold amsler grid testing: this is rapid sensitive and high yield means of assessing the central fields in patients with diabetic retinopathy

Photo stress test: after images and central scotomas persist after long time. This explained the prolonged re adaptation time in photo stress test in the affected eye

ELECTROPHYSIOLOGY

Electro Retinography:

Early stages of diabetic retinopathy may reveal abnormalities of oscillatory potential in the ascending limit of b-wave. Delay in implicit time occurs as macular odema progresses

Electrooculography:

This test may reveal abnormal light to dark ratio (arden ratio)

Visually evoked responses:

The macular disease with odema the VER shows amplitude reduction depending on the visual acuity with no change in latency

Fundus fluorescein angiography:

This is one of the mandatory investigations needed in macular odema:

1. Confirmation of diagnosis
2. Documentation of lesion
3. Deciding about the management
4. Follow up

OCT

This investigation modality can be used for diagnosis and follow up. It is non invasive technique can quantify the macular thickness

1. Spongy odema: It is mostly confined to outer retinal layers due to back scattering from intraretinal fluid
2. Cystoid odema: The cystoid spaces are confined to outer retina mostly. In long standing cases they fuse to form large cyst.
3. Serous detachment:It is seen as a hypo reflective space below the fovea. It may disappear following laser
4. Taut posterior hyaloid membrane
5. Vitreomacular traction:

Evolving therapies for clinically significant macular odema

1. Laser photocoagulation

The goal of Laser photocoagulation for DME is to limit vascular leakage through focal laser burns of leaking microaneurysms or grid laser burns in areas of diffuse break down of blood retinal barrier.

Moderate visual loss was reduced by 50% in patients who received laser therapy in the ETDRS. Double frequency Nd:YAG lasers (532nm) is the lasers of choice in the management of DME. The

Treatment strategy given by ETDRS is to photocoagulate all leaking microaneurysms further than 500u from the centre of macula and to place grid of 50 -100um burns in areas of capillary leakage and in areas of capillary non perfusion. Complications are RPE atrophy, laser scars, sub retinal fibrosis can lead to visual loss.

Focal laser for micro aneurysms or grid photocoagulation in diffuse macular odema where leakage from capillaries. The Early Treatment for Diabetic Retinopathy Study(ETDRS) established the indications and guidelines for laser treatment in DME. Laser Treatment is indicated for CSME which is defined by atleast one of the following:

- Thickening of the retina< 500 microns from the center of the macula

- Hard exudates with thickening of the adjacent retina located 500 microns from the center of the macula
- A zone of retinal thickening, 1 disc area or larger in size located 1 disc diameter from the center of the macula

2. Intravitreal corticosteroid

The rationale for the use of corticosteroids in CSME is it stabilises blood retinal barrier. It inhibits VEGF and other Cytokines growth factors that regulate endothelial tight cell junctions. They also reduce the synthesis of prostaglandins and leukotrine, two potent inflammatory mediators. The resultant anti inflammatory effect contributes to the reduction of macular odema. Increased diffusion by modulation of calcium channels could also account for the efficacy of corticosteroids reducing of macular odema. IVTA reduces retinal thickeneing on OCT and improves vision in a substantial number of patients. Patients with cystoids macular odema respond better.

However duration of effect varies and visual decline are often observed 4 to 6 months after injection. Repeated therapy is often limited by side effects. Intraocular pressure elevation occurs in about one third of patients. Acceleration of cataract formation, endophthalmitis and retinal detachment are the other complications.

3. Intravitreal anti VEGF agents

Anti VEGF agents work to restore the normal permeability of blood retinal barrier.VEGF increases vascular permeability by relaxing endothelial junctions. Inhibition of VEGF blocks this effect to some extent.

Ranibizumab (lucentis) is a humanized antigen binding fragment(Fab) of a second generation, recombinant monoclonal antibody directed against VEGF. It has high specificity and affinity for all soluble human isoforms of VEGF.

Bevacizumab (avastin) is a full length humanized monoclonal antibody for treatment of metastatic colorectal cancer, Intravitreal formulation was first used off label for the treatment of age related macular degeneration. In cases of diffuse odema that failed other treatments, Intravitreal injection of Bevacizumab was associated with improved vision and decreased retinal thickness 12 weeks after the first injection. Pegatanib sodium (macugen) is an anti VEGFaptamer blocks the effect of VEGF-165

4. Protein kinase C Inhibitor

Protein kinase C is upregulated in hyperglycemia in multiple tissues vascular endothelial cells. Oral administration of ruboxistaurin 32mg/day over a period of 36 months have demonstrated the efficacy in prevention of sustained moderate vision loss in non proliferative diabetic retinopathy by reducing the macular odema within 100 microns from the centre of the macula and the need for intial laser treatment .

PART - II

AIM OF THE STUDY

PRIMARY OBJECTIVE

1. To assess the improvement in contrast sensitivity with

   Pelli Robson chart after grid laser

2. To quantify assessment of macular thickness by OCT.

SECONDARY OBJECTIVE

To assess the improvement in visual acuity with ETDRS chart after grid laser.

SAMPLE SIZE

A total of 50 patients were studied.

INCLUSION CRITERIA

1. Patients with Non Proliferative Diabetic Retinopathy with Clinically significant macular odema (CSME)

2. Visual acuity 6/24 or better

EXCLUSION CRITERIA

1. Psuedophakia
2. Age related macular degeneration
3. Glaucoma
4. Proliferative diabetic retinopathy
5. Post pan retinal photocoagulation
6. Ischemic maculopathy

MATERIALS AND METHODS

This study was intended to evaluate the efficacy of grid laser photo coagulation on contrast sensitivity in patients with CSME which was carried out in the department of Retina services of RIOGOH, Chennai from June 2010 to June 2011. All the patients who were referred to retina clinic with Diabetic CSME were screened and selected for the study.

Detailed history was taken from all the patients regarding the duration and treatment for Diabetes. Contrast sensitivity is recorded with Pelli- Robson chart.Visual acuity recorded with ETDRS chart. Intra Ocular Pressure is measured by applanation tonometry. Anterior segment examination with slit lamp biomicroscopy was done. Posterior segment examination with 90 D, binocular Indirect opthalmoscope and a detailed fundus drawings were done and fundus photo was taken for documentation. Fundus flourescin angiography (FFA) and Optical coherence topography(OCT) were done for all patients. Biochemical marker HBA1C level was documented. These patients are treated with grid laser and followed up over 3 months Grid laser done for patients with diffuse macular odema using double frequency Nd yag laser 532nm. The parameters of grid laser are:

Duration- 100- 200ms

Spot size- 50 – 100 u

Intensity-mild to moderate

One burn width apart,500u from centre of macula and 500u from temporal margin of disc.

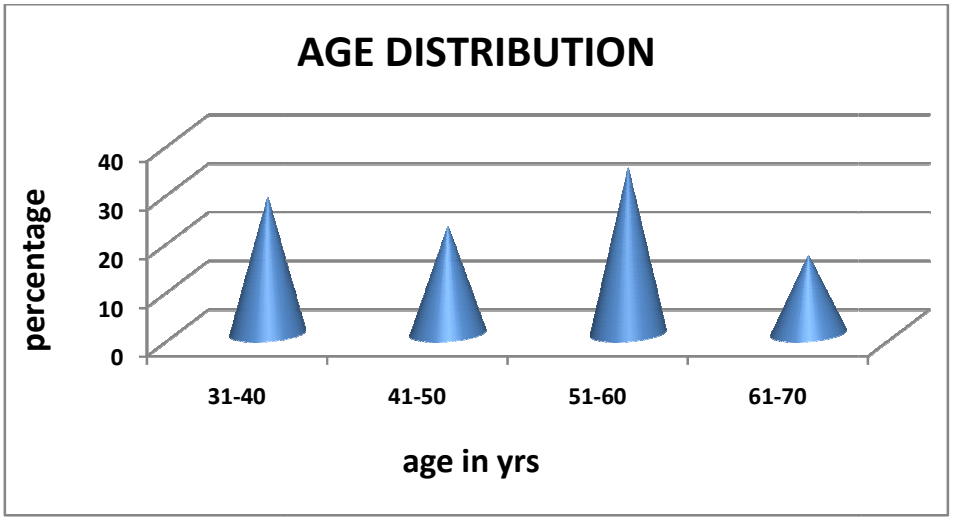
Guidelines for Follow up:

Patients were followed up over a period of 4 weeks, 8 weeks, 12 weeks for improvement in contrast sensitivity with pelli robson chart, visual acuity by ETDRS chart during follow up. Quantitative analysis of macula thickness was documented by OCT.

OBSERVATIONS AND RESULTS

Table 1: Age distribution

Age distribution	No of patients	Percentage
31 - 40	**14**	**28**
41 - 50	**11**	**22**
51 -60	**17**	**34**
61 - 70	**8**	**16**



Most of the patients in our study were in the age group of 51 -60 yrs (34%)

Table 2: Sex distribution

Sex	No of patients	Percentage
Male	**32**	**64**
Female	**18**	**36**

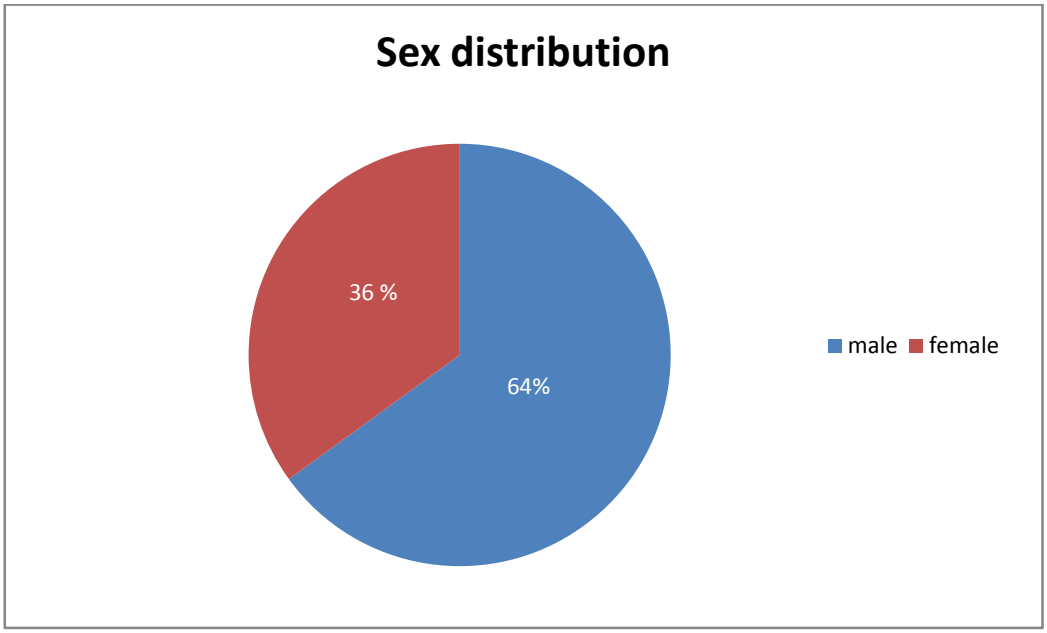


Table 3.1: Results of visual acuity by ETDRS chart (after 3 months)

No of letters improved on ETDRS chart	ETDRS Score = no of letters read plus 30 at distance of 4m	Eyes
5 letters	Score from 40 to 45	10
	Score from 45 to 50	22
	Score from 50 to 55	22
	Score from 55 to 60	10
	Score from 60 to 65	2
10 letters	Score from 45 to 55	14
	Score from 50 to 60	6
15 letters	Score from 50 to 65	4
No improvement	Score from 45 to 45	8
	Score from 50 to 50	2

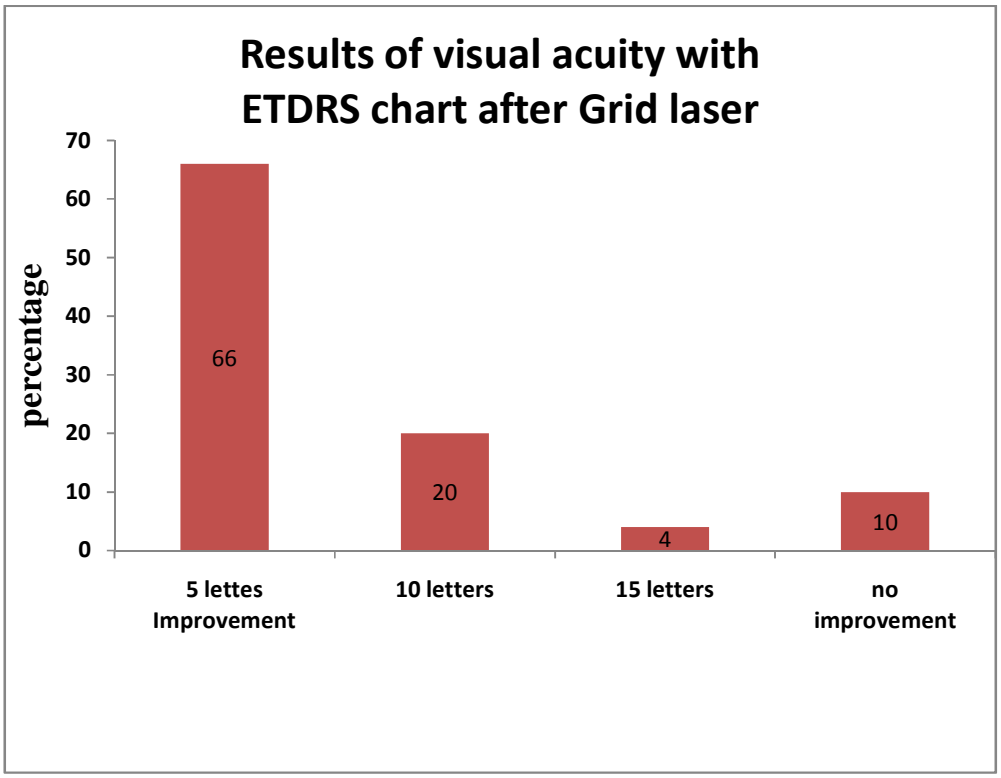


Table 3.2 Results of visual acuity by ETDRS chart (after 3months)

RESULTS	EYES
Improvement	90
5 letters	66
10 letters	20
15 letters	4
No Improvement	10

There was improvement in 90 eyes in the treated eyes, where as 10 eyes did not show any improvement. With 66% showing 5 letters improvement, 20% showing 5 letters improvement, 4% showing 15 letters improvement aft 12 weeks of grid laser. By chi- square test P value was <0.0001 which was statistically significant

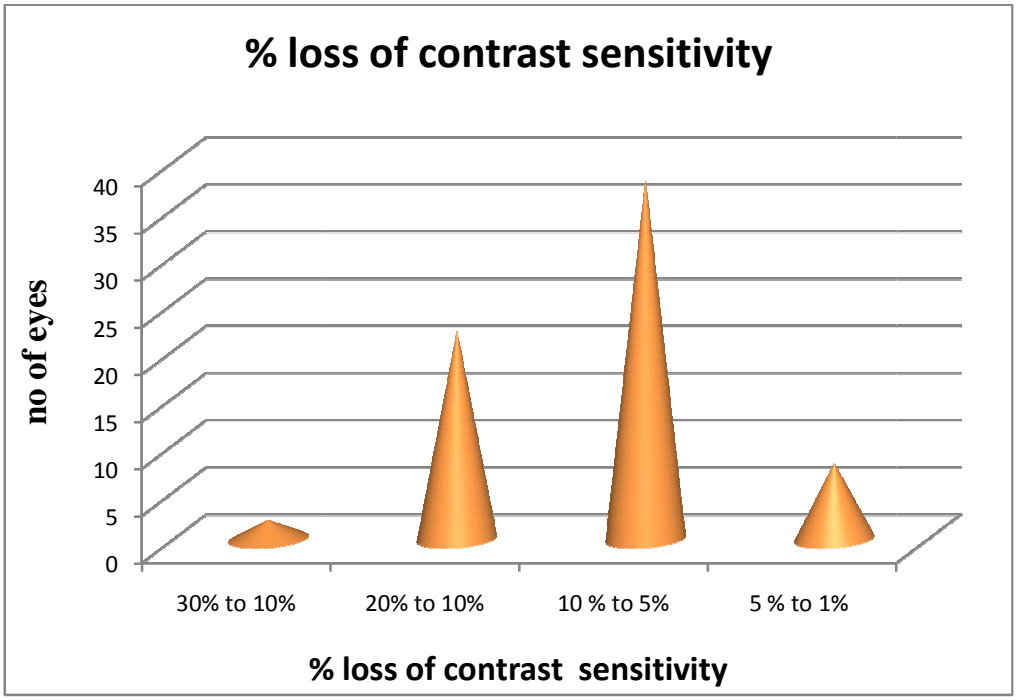
Table 4.1: Results of Improvement of Contrast sensitivity in Pelli Robson chart

Improvement assessed by % loss of contrast sensitivity	Eyes
From 30% loss to 20%	2
From 20% loss to 10%	22
From 10% loss to 5%	38
From 5% loss to 1%	8

Table 4.2: Results of Contrast sensitivity

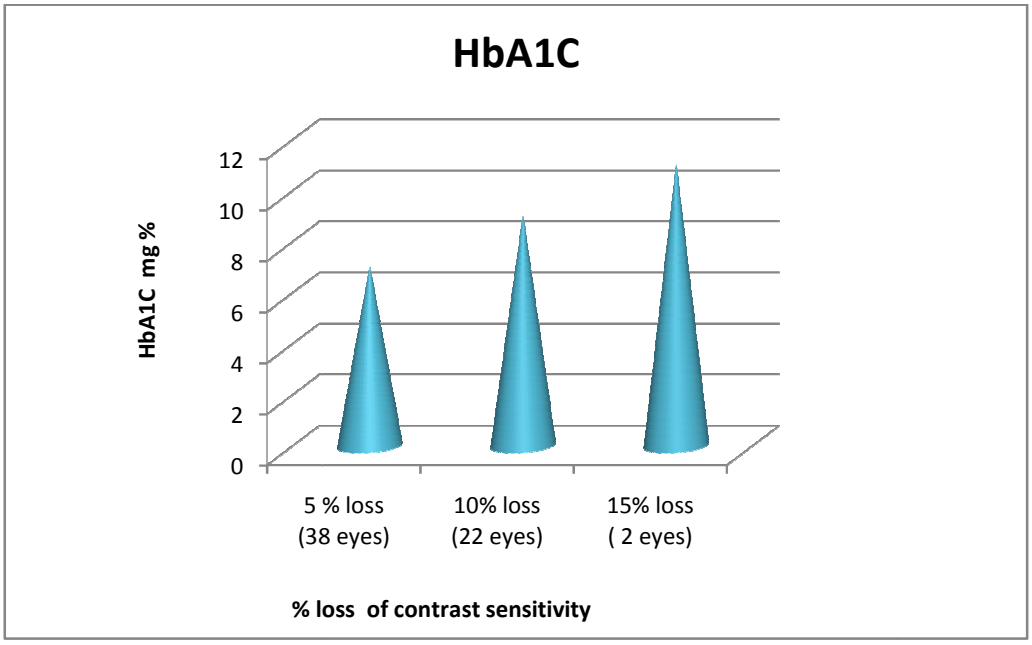
Results	eyes
Improvement	70
No improvedment	30

Results of contrast sensitivity after Grid laser treatment



In our study there was improvement in contrast sensitivity in 70% of patients, 30% didnot show improvement. Among the patients who improved 2 eyes had improvement with loss of contrast sensitivity from 30% to 20%. 22 eyes showed improvement from 20% loss to 10%. 38 eyes showed improvement from 10% loss to 5%. 8 eyes showed improvement from 5% loss to 1%.By chi- square test P value was <0.0001 which was statistically significant.

Correlation of HbAIC with contrast sensitivity

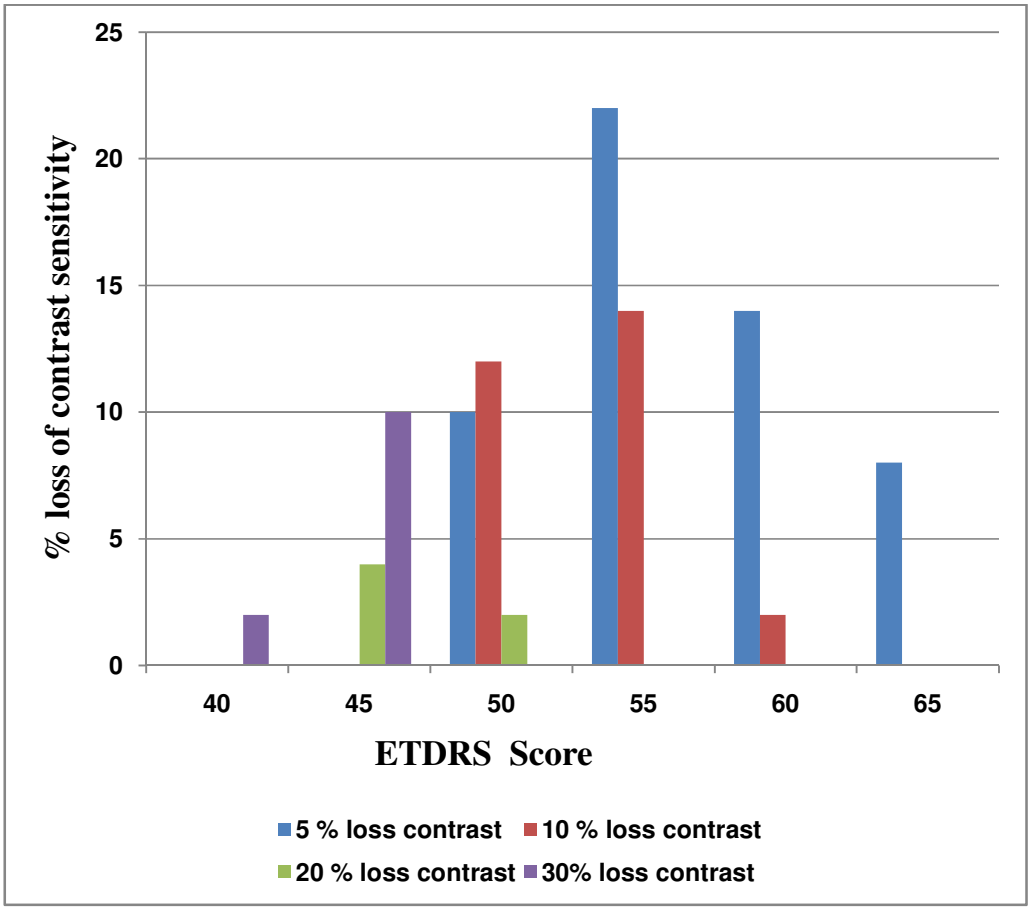


Most of our patients with good glycemic control of HbA1C value of 6-8 mg% had 5 % loss of contrast sensitivity. 22 eyes had value of 8-10 mg%, had 10 % loss of contrast sensitivity 2 eyes with 15% loss of contrast sensitivity had HbA1C of 10 –12mg% with poor glycemic control.

Table-5 Correlation of contrast sensitivity with visual acuity

	% loss of Contrast sensitivity						Total
ETDRS SCORE	**1 %**	**5 %**	**10 %**	**20 %**	**30 %**	**50 %**	
40	0	0	0	0	0	2	2
45	0	0	0	4	10	0	14
50	0	10	12	2	0	0	21
55	0	22	14	0	0	0	36
60	6	8	2	0	0	0	16
65	2	6	0	0	0	0	8
Total	**8**	**46**	**28**	**6**	**10**	**2**	**100**

Correlation of contrast sensitivity with visual acuity



2 eyes with ETDRS score of 40 had 50% loss of contrast sensitivity, 4 eyes with score of 45 had 20% loss of contrast sensitivity, 10 eyes had 50% loss of contrast sensitivity. 10 eyes with score of 50 had 5% loss of contrast sensitivity and 12 eyes had 10% loss of contrast sensitivity. 8 eyes with score of 60 had 5% loss of contrast sensitivity. The chi-square test had P value < 0.0001 which was statistically significant.

Table -6 FFA findings showing pattern of leakage

FFA Pattern	EYES
FOCAL LEAK	35
DIFFUSE LEAK	48
MIXED PATTERN	17

Most of the patients in the study 48 eyes had diffuse pattern of leakage, 35 eyes had focal leakage, 17 eyes had mixed pattern leakage. Ischaemic maculopathy was excluded from the study as laser was not indicated for such patients.

Table -7 OCT findings in patients

OCT FINDINGS	EYES
CYSTOID ODEMA	28
SPONGY ODEMA	48
SUBFOVEAL DETACHMENT	16

1

Most of the patients in our study included spongy type of macular odema (48 eyes) , cystoid odema in 28 eyes, subfoveal detachment in 16 eyes.

Grid laser photocoagulation

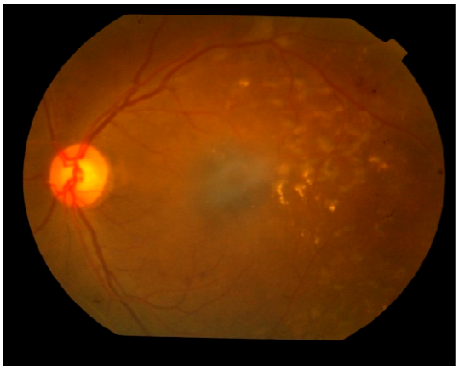


Fig13 Fundus picture showing grid laser marks

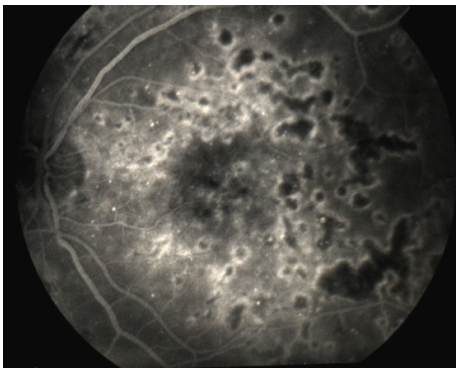


Fig 14 FFA showing hyperflourescent lesion in the centre and hyperflourescent lesion around it.

OCT FINDING IN SPONGY ODEMA

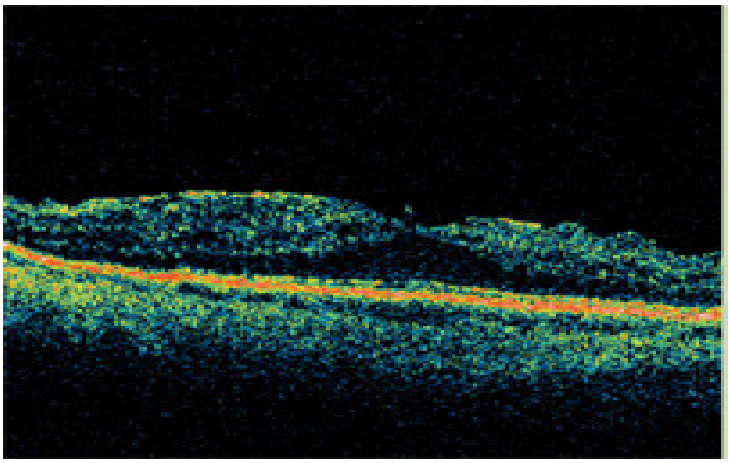


Fig 15 Pre treatment of spongy edema

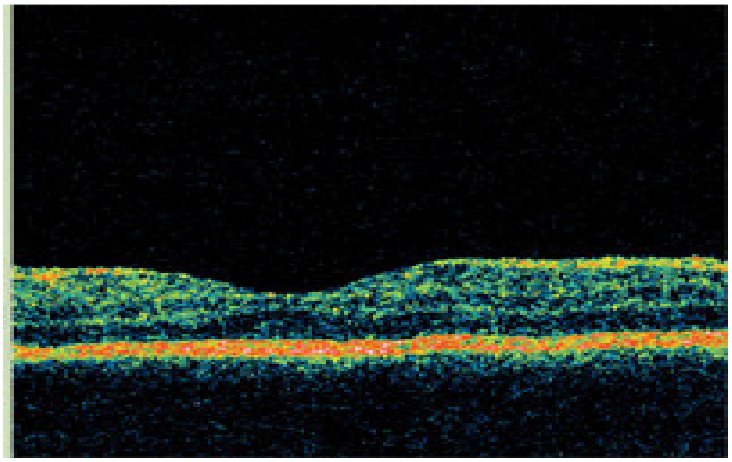


Fig 16 Post grid laser treatment showing the reduction in thickness

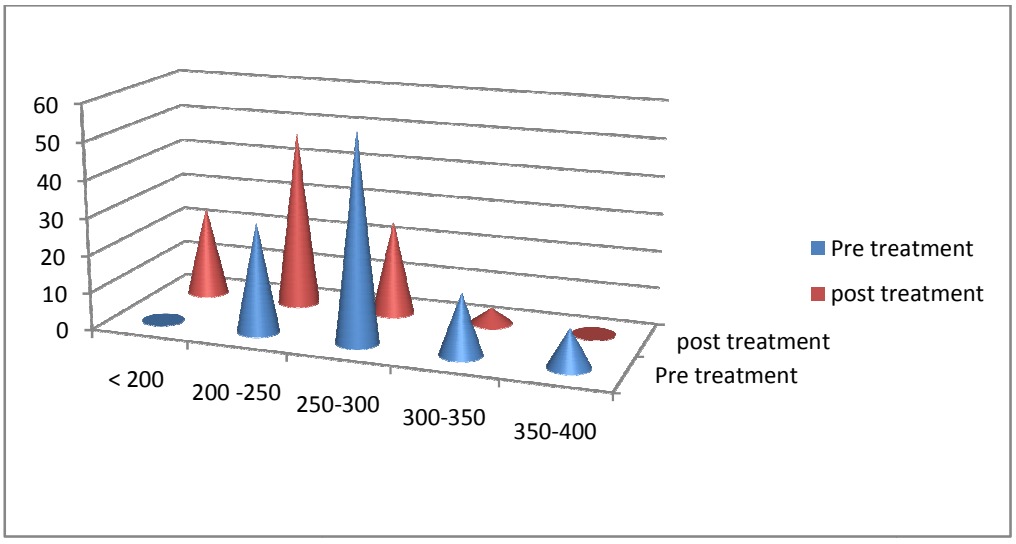
Table 8.1- Pre treatment macular thickness

MACULAR THICKNESS (microns)	EYES
200 -250	29
250- 300	45
300- 350	16
350- 400	10

Table 8.2- Post treatment macular thickness

MACULAR THICKNESS (microns)	EYES
<200	24
200- 250	47
250 -300	25
300- 350	4

Comparison between pre and post treatment macular thickness by OCT after Grid laser



Macular thickness showed significant improvement. Prior to treatment 71 % patients had thickness more than 250 microns Post treatment all patients had macular thickness less than 350 microns. However reduction in macular thickness didnot correspond to an equivalent increase in visual acuity and contrast sensitivity could be due to long standing macular odema which leads to photoreceptor damage. By chi- square test P value was < 0.0001 which was statistically significant.

DISCUSSION

This study included 100 eyes of 50 patients in RIOGOH from June 2009 to June 2011.

Age distribution

Most of the patient in our study were in the age group of 51-60yrs (34%)

Sex distribution

In our study male patients were 62 % and remaining 36% being females.

Visual acuity by ETDRS chart

There was improvement in 90 eyes in the treated eyes, where as 10 eyes did not show any improvement. With 66% showing 5 letters improvement, 20% showing 5 letters improvement, 4% showing 15 letters improvement aft 12 weeks of grid laser. As per ETDRS study there was reduction in the moderate visual loss. By chi- square test P value was < 0.0001 which was statistically significant.

Contrast sensitivity by Pelli Robson chart

In our study there was improvement in contrast sensitivity in 70 eyes. And 30 eyes didnot show improvement. Among patients who didnot improvement, 9 patients(18 eyes) had poor glycemic control, 3 patients (6 eyes) had hard exudate on the fovea and 3 patients (6 eyes) had chronic persistent CSME. By chi- square test P value was < 0.0001 which was statistically significant.

Correlation of contrast sensitivity with visual acuity

Contrast sensitivity can be impaired even in the presence of normal visual acuity. As per study visual acuity with 6/24 or better only were included in the study.2 eyes with ETDRS score of 40 had 50% loss of contrast sensitivity, 4 eyes with score of 45 had 20% loss of contrast sensitivity, 10 eyes had 50% loss of contrast sensitivity. 10 eyes with score of 50 had 5% loss of contrast sensitivity and 12 eyes had 10% loss of contrast sensitivity. 8 eyes with score of 60 had 5% loss of contrast sensitivity. There is no significant association between visual acuity and Contrast sensitivity.

Macular thickness in OCT

Macular thickness showed significant improvement. Prior to treatment 71 % patients had thickness more than 250 microns. Post treatment all patients had macular thickness less than 350 microns. However reduction in macular thickness didnot correspond to an equivalent increase in visual acuity and contrast sensitivity could be due to long standing macular odema which leads to photoreceptor damage

CONCLUSION

Contrast sensitivity is an important aspect of visual function and is even more important for ordinary daily tasks than visual acuity. Loss of Contrast sensitivity is more important and disturbing for the patient than is the loss of visual acuity

Visual acuity was recorded by ETDRS chart due to the fallacies associated in Snellen shart. The Contrast sensitivity was recorded by Pelli Robson's chart was sensitive and reproducible.

Grid laser photocoagulation in CSME helps in improving the contrast sensitivity and stabilizes the visual acuity.

The changes in contrast sensitivity and visual acuity are independent of each other.

PART III

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PROFORMA

Name

Age

Sex

Occupation

OP no

Address

Phone no

Chief complaints

H/o defective vision

H/o distorted vision

Past history

Diabetes – duration

TypeI/II

Drug

PRP

Hypertension- duration

Medication

Associated IHD, hyperlipidemia

H/o cataract surgery in the past

General physical examination

PR CVS

BP RS

Ocular examination

	RE	LE
Visual acuity by Snellen		
Visual acuity by ETDRS		
IOP by applanation		
Contrast sensitivity by Pelli Robson chart		
Conjunctiva		
Cornea		
Iris		
Ant chamber		
Lens		
Slit lamp examination		
Fundus by 90D, IDO		

Fundus flourescein angiography

Optical coherence tomography

Investigations

FBS, PPBS, HbA1c,

Lipid profile

Renal function test

Diagnosis

Treatment: grid laser photocoagulation

Power, Spot size, duration

Follow up and outcome of the treatment

KEY TO MASTER CHART

Vn	-	vision
pH	-	pin Hole
Nip	-	not improving with pin hole
M	-	Male
F	-	Female
ETDRS	-	Early Treatment Diabetic Retinopathy Study
NPDR	-	Non proliferative diabetic retinopathy
CSME	-	Clinically significant macular odema
OCT	-	Optical coherence tomography

MASTER CHART

SL NO	name	age	sex	Diagnosis with CSME	PRE TREATMENT								POST TREATMENT							
					Vn snellen		ETDRS score		contrast sensitivity		OCT macular thickness		Vn snellen		ETDRS Scores		contrast sensitivity		OCT macular thickness	
					RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE
1		60	m	be severe NPDR	6/24 NIP	6/24 ph 6/18	45	50	30	20	370	290	6/24 ph 6/18	6/24 ph 6/18	45	45	20	20	306	260
2	sekar	45	m	be moderate NPDR	6/12 ph 6/9	6/12 ph 6/9	50	50	20	20	240	240	6/12 ph 6/9	6/12 ph 6/9	55	55	10	10	200	200
3	saroja	55	f	be moderate NPDR	6/18 nip	6/12 ph 6/9	50	50	20	20	362	275	6/12 nip	6/9 nip	55	55	10	10	260	240
4	hamsapathy	59	m	be severe NPDR	6/24 nip	6/24 nip	45	45	30	30	290	290	6/24 nip	6/24 nip	45	45	30	30	260	260
5	lalitha	35	f	be mild NPDR	6/12 ph 6/9	6/12 ph 6/9	55	55	10	10	240	240	6/12 ph 6/9	6/12 ph 6/9	60	60	5	5	180	180
6	Gopinath	39	m	be mild NPDR	6/12 ph 6/9	6/12 ph 6/9	55	55	10	10	280	260	6/12 ph 6/9	6/12 ph 6/9	60	60	5	5	210	210
7	kuppammal	60	f	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	50	50	20	20	390	390	6/12 NIP	6/12 NIP	55	55	10	10	240	240
8	andal	55	f	be severe NPDR	6 / 24 NIP	6 / 24 ph 6/18	45	45	30	30	368	338	6/24 NIP	6/24 ph 6/18	45	45	30	30	246	260
9	Marimuthu	58	m	be severe NPDR	6/24 ph 6/18	6/24 ph 6/18	45	45	20	20	355	350	6/24 ph 6/18	6/24 ph 6/18	50	50	10	10	295	250
10	kumari	37	f	be mild NPDR	6/9 nip	6/12 ph 6/9	60	60	5	5	260	260	6/9 ph 6/6	6/9 ph 6/6	65	65	5	5	200	200
11	gunasundari	58	f	be moderate NPDR	6/18 nip	6/18 ph 6/9	45	45	20	20	280	280	6/18 ph 6/9	6/18 ph 6/9	50	50	10	10	246	246
12	venkatesan	34	m	be moderate NPDR	6/12 ph 6/9	6/12 ph 6/9	50	50	10	10	334	334	6/12 ph 6/6	6/12 ph 6/6	55	55	5	5	278	278
13	gangadharan	66	m	be moderate NPDR	6/24 nip	6/18 ph 6/12	40	40	50	50	220	370	6/24nip	6/24nip	40	40	50	50	220	320
14	ramanathan	40	m	be severe NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	278	258	6/18 ph 6/9	6/18 ph 6/9	50	50	5	5	218	218
15	selvaraj	56	m	be severe NPDR	6/24 ph 6/18	6/24 ph 6/18	45	45	10	10	358	378	6/18 ph 6/9	6/18 nip	50	50	10	5	215	265
16	amudha	36	f	be severe NPDR	6/24 ph 6/18	6/24 ph 6/18	50	50	20	20	306	326	6/18 ph 6/9	6/18 ph 6/9	50	50	20	20	270	260
17	sudha	44	f	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	50	50	10	10	340	310	6/12 nip	6/12 nip	55	55	5	5	286	266
18	johnson david	46	m	be moderate NPDR	6/24 ph 6/12	6/24 ph 6/12	45	45	10	10	280	280	6/12 ph 6/9	6/12 ph 6/9	50	50	5	5	216	206
19	sambandam	62	m	be severe NPDR	6/24 NIP	6/18 ph 6/12	40	40	30	30	326	356	6/24 nip	6/24 nip	45	45	30	30	310	330
20	ragavan	40	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	260	274	6/12 ph 6/9	6/12 ph 6/9	55	55	5	5	190	220
21	durai	57	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	256	246	6/12 ph 6/9	6/12 ph 6/9	55	55	5	5	216	206
22	elumalai	45	m	be mild NPDR	6/9 ph 6/6	6/9 ph 6/6	55	55	5	5	248	228	6/9 ph 6/6	6/9 ph 6/6	60	60	5	5	200	200
23	paneerselvam	57	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	5	5	289	250	6/12 ph 6/9	6/12 ph 6/9	55	55	5	5	210	210
24	suguna	40	f	be mild NPDR	6/9 ph 6/6	6/9 ph 6/6	50	50	5	5	220	220	6/6 p	6/6 p	60	60	1	1	190	190
25	rukmani	56	f	be severe NPDR	6/24 ph 6/18	6/24 nip	45	45	10	10	316	316	6/18 ph 6/9	6/18 ph 6/9	50	50	5	5	278	278
26	subramani	62	m	be severe NPDR	6/24 nip	6/18 ph 6/12	40	40	30	30	375	388	6/24 nip	6/24 nip	45	45	30	30	280	280
27	jayaprakash	64	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	285	275	6/12 ph 6/9	6/12 ph 6/9	50	50	5	5	220	226
28	anwar	58	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	246	264	6/9 ph 6/6	6/9 ph 6/6	55	55	5	5	190	200
29	shakil ahmed	44	m	be mild NPDR	6/6 p	6/6 p	60	60	5	5	210	200	6/6 p	6/6 p	65	65	5	5	180	188
30	vimala	60	f	be severe NPDR	6/24 ph 6/12	6/24 ph 6/12	45	45	20	20	290	280	6/18 ph 6/12	6/18 ph 6/12	50	50	10	10	220	227
31	amwar	58	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	50	50	10	10	265	268	6/18 ph 5/9	6/18 ph 5/9	55	55	5	5	216	218
32	pushpa	45	f	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	50	50	20	20	286	268	6/12 ph 6/9	6/12 ph 6/9	55	55	10	10	210	230
33	vijaya	48	f	be severe NPDR	6/24 ph 6/18	6/24 ph 6/18	45	45	20	20	266	266	6/18 ph 6/12	6/18 ph 6/12	55	55	10	10	206	206
34	balammal	54	f	be moderate NPDR	6/18 ph 6/12	6/12 nip	50	50	20	20	250	340	6/12 ph 6/9	6/12 nip	55	55	10	10	188	228
35	dasappan	35	m	be mild NPDR	6/6 p	6/6 p	55	55	5	5	218	218	6/6 p	6/6 p	60	60	1	1	192	190
36	murugan	62	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	10	10	279	269	6/12 ph 6/9	6/12 ph 6/9	50	50	5	5	216	226
37	chandra	50	m	be mild NPDR	6/18 ph 6/6p	6/18 ph 6/6p	50	50	10	10	235	232	6/6 p	6/6 p	55	55	5	5	214	204
38	perumal	65	m	be severe NPDR	6/24 ph 6/18	6/18 ph 6/6p	45	45	20	20	274	264	6/18 ph 6/12	6/18 ph 6/12	50	50	10	10	256	236
39	bhaskar	35	m	be mild NPDR	6/6 p	6/6 p	55	55	5	5	215	225	6/6 p	6/6 p	60	60	5	5	196	195
40	varadhan	40	m	be mild NPDR	6/9 nip	6/9 nip	50	50	5	5	210	210	6/6 p	6/6 p	60	60	1	1	193	195
41	kanniammal	65	f	be severe NPDR	6/24 NIP	6/18 ph 6/12p	40	40	30	30	264	264	6/24 ph 6/18	6/24 ph 6/18	45	45	30	30	256	256
42	jayagopal	34	m	be mild NPDR	6/9 ph 6/6	6/9 ph 6/6	50	50	10	10	230	230	6/6 p	6/6 p	65	65	5	5	190	190
43	krishnaveni	44	f	be moderate NPDR	6/12 ph 6/9	6/12 ph 6/9	45	45	10	10	246	246	6/6 p	6/6 p	55	55	5	5	200	200
44	vellaiyan	62	m	be severe NPDR	6/24 ph 6/18	6/24 ph 6/18	40	40	20	20	298	265	6/24 ph 6/12	6/24 ph 6/12	45	45	20	20	280	240
45	lakshmi	39	f	be mild NPDR	6/12 ph 6/9	6/12 nip	50	50	10	10	215	200	6/9 ph 6/6	6/9 ph 6/6	60	60	10	10	188	180
46	sundarajan	55	m	be moderate NPDR	6/18 ph 6/12	6/18 ph 6/12	45	45	20	20	272	282	6/12 ph 6/9	6/12 ph 6/9	55	55	10	10	234	254
47	shanthi	37	f	be mild NPDR	6/9 ph 6/6	6/9 ph 6/6	50	50	5	5	248	230	6/6 p	6/6 p	65	65	1	1	220	210
48	padmavathy	44	m	be moderate NPDR	6/12 ph 6/9	6/18 ph 6/12	45	45	20	20	266	278	6/9 nip	6/9 nip	50	50	10	10	225	255
49	gunasekaran	57	m	be moderate NPDR	6/18 ph 6/12	6/12 ph 6/9	50	50	10	10	288	260	6/12 ph 6/9	6/12 ph 6/9	55	55	5	5	214	204
50	narayanan	50	m	be moderate NPDR	6/18 ph 6/12	6/18 nip	50	50	10	10	310	300	6/12 ph 6/9	6/12 ph 6/9	55	55	5	5	280	270